REMARKS

I. Status of the Claims

Claims 275, 289, 290 and 296-301 were pending and examined in the July 9, 2010 Office Action. Claims 289, 290 and 298-301 were withdrawn and claims 275, 296 and 297 were examined therein. No claim amendments are made herewith. Claims 275, 296 and 297 are presented for reconsideration.

II. Rejections under 35 U.S.C. § 102

Claims 275 and 296 are rejected under 32 U.S.C. 102(e) as anticipated by Cantor et al. (US 5,561,043). Applicants request reconsideration and withdrawal of this rejection in light of the following discussion.

The instant claims are directed to

> An isolated multimeric composition comprising a binding matrix and more than one monomeric unit, wherein each monomeric unit comprises two elements covalently attached to one another, wherein a first element is a protein, wherein said protein is a ligand to a cell surface receptor, wherein a second element is a single-stranded polynucleotide and wherein each monomeric unit is separately attached to said binding matrix through said second element via hydrogen bonding between said single-stranded polynucleotide of said monomeric unit and said binding matrix, wherein said binding matrix is a polynucleotide, comprising sequences complementary to said single-stranded polynucleotide.

Claim 275. By contrast, Cantor et al. describe a first multimeric nucleic acid construct that comprises a functional group, which may be a protein. This construct may be hybridized to a second multimeric nucleic acid construct. However, Cantor et al. do not describe a binding matrix that is a polynucleotide, as claimed, since Cantor et al. only describe the first multimeric nucleic acid construct hybridizing to a multimeric nucleic acid, not a single polynucleotide, as claimed. As such, Cantor et al. do not describe each element of the instant claims because Cantor et al. do not teach or suggest a single binding matrix that is hybridized to multiple monomeric units. Rather, Cantor et al. only teach multimeric complexes where a single nucleic acid has only one other nucleic acid hybridized to it.

Based on the above discussion, it is clear that Cantor et al. do not teach or suggest every element of the instant claims, and thus do not anticipate the claims. Applicants therefore respectfully request withdrawal of the rejection under 35 U.S.C. 102(e).

III. Rejections under 35 U.S.C. § 103

(a) Claims 275 and 296-297 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al. (described under **II.** above) in view of Osborne et al. (PNAS, 1976;73:4536-4540). The Office Action asserts that Cantor et al. teach all elements of the claims except that hormones include insulin, which is taught by Osborne et al. Applicants respectfully request reconsideration and withdrawal of this rejection in light of the following comments.

As discussed under **II.** above, Cantor et al. do not teach or suggest a binding matrix that is a polynucleotide, since all constructs described by Cantor et al. comprise a second multimeric nucleic acid that hybridizes to a first multimeric nucleic acid comprising a functional group. Osborne et al. also do not teach or suggest a binding matrix that is a polynucleotide. As such, the combination of references do not teach or suggest all of the claim elements and therefore do not make the instant claims obvious. Withdrawal of this rejection is therefore respectfully requested.

(b) Claims 275 and 296-297 are rejected under 35 U.S.C. 103(a) as being unpatentable over Priest (US 5,391,723) in view of Osborne et al. (described under **(a)** above). The Office Action asserts that Priest teaches all elements of the claims except (i) a multimer of the monomeric units recited in the instant claims, and (ii) that insulin can be a targeting molecule. However, the Office Action further asserts that Osborne et al. teach the latter and the former is an obvious variation "[s]ince making a composite composition comprising more than one such monomer structure is a logical option for various purposes (e.g., multimerization of insulin for experimental purposes)." Office

Action at p. 6. Applicants respectfully request reconsideration and withdrawal of this rejection in light of the following comments.

> Priest describes conjugates comprising
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> ...a targeting protein bound (preferably covalently) to a linking group, which in turn is bound (preferably covalently) to an oligonucleotide strand that can be a single strand or a duplex.... The oligonucleotide strand can bind to a complementary strand to form a duplex that is capable of binding therapeutic agents....

Priest, col. 2, lines 32-40. The purpose of these conjugates is to target a cytotoxic therapeutic agent to cells to be selectively killed, avoiding killing nontargeted cells. See, e.g., Priest, Background of the Invention (col. 1); col. 2, lines 3-8; and col. 7, lines 3-12.

While the Office Action acknowledges that Priest does not teach or suggest multimers of the targeting protein-linking group-oligonucleotide bound to a complementary strand, the Office Action asserts that such multimers are logical options. Applicants disagree, and assert that Priest does not teach or suggest such multimers because the skilled artisan would understand that such multimers would have no use for the purpose described by Priest, since only one targeting molecule is sufficient to deliver the conjugate to its target and more than one targeting molecule would not improve the targeting ability of the conjugate. Thus, although the Office Action suggests, by citing *In re Kerkhoven* T pp. 6-7, that the Priest composition and the composition of the instant claims are "taught by the prior art to be useful for the same purpose" the Priest conjugates in fact have a very different purpose than the instantly claimed compositions, since the Priest conjugates have the purpose of directing a cytotoxic therapeutic agent to targeted cells, whereas the instantly claimed compositions have as one purpose the binding of multiple ligands to multiple cell surface receptors to increase the activation of the receptor resulting therefrom. As such, the skilled artisan would understand that multimers of the targeting protein-linking group-oligonucleotide bound to a complementary strand is not obvious from Priest, since such multimers would serve no purpose. Indeed, such multimers would be understood to be counterproductive to the purpose of the Priest conjugates, since such

a multimeric structure would be larger than the single targeting protein-linking group-oligonucleotide bound to a complementary strand as taught by Priest and the larger structure would make the internalization of the conjugate into the cell to deliver the therapeutic compound (as described at col. 7, lines 12-23 of Priest) more difficult.

The above deficiency is not resolved by Osborne et al. since Osborne et al. provides no teaching of protein-polynucleotide conjugates.

In light of the above discussion it is clear that the combination of references do not make the instant claims obvious since that combination would not suggest to the skilled artisan that multimers of Priest's targeting protein-linking group-oligonucleotide could usefully be bound to a complementary strand. Withdrawal of this obviousness rejection is therefore respectfully requested.

IV. Double Patenting Rejections

Claims 275 and 296-297 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 246 and 264-265 of copending Application No. 08/978,632. Since this rejection is dependent on the scope of the final claims in both the instant application and application 08/978,632, Applicants will provide a terminal disclaimer where necessary when a proper ODP rejection is the only rejection remaining in this application.

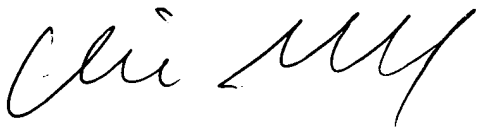
V. Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of the rejections of record and examination of withdrawn claims 289, 290, and 298-301, as provided under MPEP 821.04, since the withdrawn claims have all the limitations of allowable claim 275.

Applicants authorize the United States Patent and Trademark Office to charge all fees required to maintain pendency of this application, including the extension of time and Request for Continued Examination fees to Deposit Account No. 05-1135.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the number provided below.

Respectfully submitted,



Elie Gendloff
Registration No. 44,704
Attorney for Applicants

ENZO BIOCHEM, INC.
527 Madison Avenue, 9th Floor
New York, New York 10022-4304
Telephone: (212) 583-0100
Facsimile: (212) 583-0150